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Incidence trends of viral hepatitis A, B, and C seropositivity over eight years of surveillance in Saudi Arabia

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Summary
Objectives: In Saudi Arabia, viral hepatitis ranked the second most common reportable viral disease in 2007, with almost 9000 new cases diagnosed in that year. The objective of this study was to determine the incidence trends of viral hepatitis seropositivity among the population served by the National Guard Health Affairs (NGHA) hospitals in the central, eastern, and western Saudi Arabia regions.
Methods: The surveillance system at King Abdulaziz Medical City in Riyadh receives weekly reports of laboratory confirmed hepatitis A virus (HAV), hepatitis B virus (HBV), and hepatitis C virus (HCV) cases from all NGHA-served regions. In this study the viral hepatitis surveillance data for the period from January 2000 through December 2007 were analyzed.
Results: Between 2000 and 2007, a total of 14 224 seropositive cases of viral hepatitis were reported to the surveillance system. The average annual incidence of seropositivity per 100 000 served population was highest for HBV (104.6), followed by HCV (78.4), and lowest for HAV (13.6). Saudis had higher HBV and HAV incidence, but lower HCV incidence compared to non-Saudis. Over the eight years (2000—2007), the incidence of all three viral hepatitis types showed a 20—30% declining trend. Only HAV incidence followed a clear seasonal cyclic pattern.
Conclusions: Despite the declining trend over the eight-year period, viral hepatitis, especially that caused by HBV and HCV, remains a major public health problem in Saudi Arabia, and has probably been underestimated in previous reports. There is a need for more comprehensive prevention strategies.

Introduction

Viral hepatitis is caused by infection with any of at least five distinct viruses, of which hepatitis A virus (HAV), hepatitis B

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virus (HBV), and hepatitis C virus (HCV) are the three most commonly identified worldwide. This disease represents a major public health problem in Saudi Arabia. According to the Saudi Ministry of Health (MOH) data, viral hepatitis ranked the second most common reportable viral disease after chickenpox in 2007, with almost 9000 new cases diagnosed in that year (52% HBV, 32% HCV, and 16% HAV).[1] In Saudi Arabia, HBV and HCV are major causes of disease requiring liver transplantation and of hepatocellular carcinoma, resulting in the need for considerable healthcare resources.[2–4]

The epidemiology of viral hepatitis in Saudi Arabia has undergone major changes, concurrent with major socioeconomic developments over the last two to three decades. Since the 1980s, Saudi Arabia has been known as a high HBV endemic area.[5] However, starting in 1990, HBV vaccine has been administered to all Saudi infants/children.[6] This has been associated with a reportable decline in hepatitis B surface antigen (HBsAg) seroprevalence, mainly in children.[1,6–8] HCV remains a major public health problem in Saudi Arabia, especially among certain high risk groups.[9,10] Moreover, the reported high rate of decline in HCV in some prevalence studies over the last decade[9,11] has not been confirmed in a recent large incidence report,[12] nor in the Saudi MOH data.[1] Recently, HAV vaccine has been added to the Saudi list of infant/childhood immunizations. Universal immunization against HAV in Saudi Arabia was recently recommended after a shift in the HAV epidemiology in the country, reducing it from a classic high endemic area to a low/moderate endemic area.[13,14]

With few exceptions,[6,15] the published rates of viral hepatitis in Saudi Arabia have mainly been based on prevalence studies. While these studies may be good for measuring viral hepatitis burden, they have limited ability to measure the actual disease risk in the community or the effectiveness of immunization programs. These prevalence studies are typically retrospective, have small sample sizes, evaluate selected populations, or cover localized geographic areas. Together with the different methods used, these limitations may impede the ability to study temporal trends in viral hepatitis rates. The objective of the current study was to report the incidence trends of viral hepatitis seropositivity, using a standardized methodology, for the population served by the National Guard Health Affairs (NGHA) hospitals in different regions of Saudi Arabia between 2000 and 2007.

Methods

Four NGHA hospitals (approximately 2000 beds in total) and 73 primary care centers provide medical care for almost a million National Guard employees and their dependents (spouses, children, and parents) in the central, eastern, and western regions of Saudi Arabia. The population served by the NGHA (97% Saudi) represents about 4% of the total population of Saudi Arabia (23.7 million in 2006) and has an annual growth rate of 2.9%. The care provided by the NGHA hospitals and primary care centers ranges from primary and preventive care to tertiary care.

The Department of Infection Prevention and Control at King Abdulaziz Medical City (KAMC) in Riyadh, Saudi Arabia has a surveillance system that receives weekly reports of reportable infectious diseases, including viral hepatitis caused by HAV, HBV, and HCV, from all NGHA-served regions. The surveillance methodology used was consistent throughout the study period. A case was considered 'suspected viral hepatitis' if the World Health Organization (WHO)-recommended acute viral hepatitis clinical case definition was met.[16] The case definition was considered met when there was an acute illness that typically included acute jaundice, dark urine, anorexia, malaise, extreme fatigue, and right upper quadrant tenderness. Only viral hepatitis cases that were laboratory confirmed, regardless of clinical signs and symptoms, were reported to the KAMC surveillance system. A case was considered to be HAV-positive if tests for anti-HAV immunoglobulin M (IgM) were positive, considered HBV-positive if tests for HBsAg were positive, and considered HCV-positive if tests for anti-HCV were positive, using ELISA. Seropositive cases of viral hepatitis were reported by laboratory personnel as part of intensive passive surveillance, which took place in multiple situations including the recruitment of new military or civilian employees, when medical care for a related condition was sought, during antenatal care (HBV only), in those attending hemodialysis units, in those undergoing organ transplantation or donating blood, or during the conducting of an outbreak investigation (mainly HAV).

For the purpose of this report, viral hepatitis surveillance data for the period from January 2000 through December 2007 were analyzed. Incidence trends refer to rates over time of newly diagnosed seropositive cases of viral hepatitis. The incidence rate for a specified type of viral hepatitis for a certain year and/or demographic group (gender, age group, nationality, or NGHA region of reporting) was calculated by dividing the number of reported seropositive cases for that type of viral hepatitis for that year and/or demographic group by the corresponding estimated NGHA-served population for that year and/or demographic group, then multiplied to give the rate per 100 000. The incidences over the eight years of surveillance (2000–2007) were plotted to detect any upward or downward trends. Duplicate cases (the same person reported more than one time with the same type of hepatitis) were not included in the analysis.

Epi Info software (version 6.04; CDC, Atlanta, GA, USA) was used to manage the surveillance database. Demographic characteristics including age, gender, nationality, and reporting NGHA region were compared between those with reported HAV, HBV, and HCV. Differences in incidence by demographic characteristics for each viral hepatitis type were examined. The Chi-square test was used to test for significant differences in categorical variables, while analysis of variance (ANOVA) or the Kruskal–Wallis test, as appropriate, were used to test for significant differences in continuous variables. All p-values were two-tailed. A p-value of <0.05 was considered as significant. SPSS software (version 15.0; SPSS Inc., Chicago, IL, USA) was used for all statistical analyses.

Results

During the eight years of surveillance (2000–2007), a total of 14 224 seropositive cases of viral hepatitis were reported to the KAMC surveillance system. HBV was the most frequent viral hepatitis type reported (n = 7572, 53%), followed by HCV

Table 1 Demographic characteristics of HAV, HBV, and HCV seropositive cases reported to the King Abdulaziz Medical City surveillance system between 2000 and 2007

	HAV	HBV	HCV	*p*-Value[a]
Mode of yearly rank among reportable infectious diseases	9th	2nd	3rd	$p < 0.001$[b]
Total number of cases	981	7572	5675	$p < 0.001$
Age, years (mean ± SD)	11.0 ± 10.5	37.2 ± 16.2	49.9 ± 17.2	$p < 0.001$[c]
Cases by age group, *n* (%)				
< 15 years	803 (81.9%)	162 (2.1%)	81 (1.4%)	$p < 0.001$
≥15 years	178 (18.1%)	7410 (97.9%)	5594 (98.6%)	
Cases by gender, *n* (%)				
Males	542 (55.2%)	4540 (60.0%)	2834 (49.9%)	$p < 0.001$
Females	439 (44.8%)	3032 (40.0%)	2841 (50.1%)	
Cases by nationality, *n* (%)				
Saudi	965 (98.4%)	7394 (97.6%)	5391 (95.0%)	$p < 0.001$
Non-Saudi	16 (1.6%)	182 (2.4%)	284 (5.0%)	
Cases by NGHA region, *n* (%)				
Central	584 (59.5%)	4695 (62.0%)	4118 (72.6%)	$p < 0.001$
Western	222 (22.6%)	2258 (29.8%)	1153 (20.3%)	
Eastern	175 (17.8%)	623 (8.2%)	404 (7.1%)	

HAV, hepatitis A virus; HBV, hepatitis B virus; HCV, hepatitis C virus; SD, standard deviation; NGHA, National Guard Health Affairs.
[a] Testing differences between viral hepatitis types using the Chi-square test unless stated otherwise.
[b] Kruskal–Wallis test.
[c] ANOVA (analysis of variance) test.

(*n* = 5675, 40%) and HAV (*n* = 981, 7%) (Table 1). The NGHA-served population ranged from about 816 000 in 2000 to 998 000 in 2007, with an average annual served population of 904 000 during the study period. The age of viral hepatitis cases was significantly different between the different viral types ($p < 0.001$), with HAV in the youngest (11.0 ± 10.5 years), followed by HBV (37.2 ± 16.2 years), and HCV in the oldest (49.9 ± 17.2 years) (Table 1). Those aged ≥15 years represented 18.1% of HAV cases, 97.9% of HBV cases, and 98.6% of HCV cases (Table 1). Gender, nationality, and reporting NGHA region were significantly different between the different types of viral hepatitis ($p < 0.001$ for each). The majority of HBV and HAV, but not HCV cases, were male. The majority of hepatitis cases were reported in those of Saudi nationality, and the majority of cases were reported from the Central NGHA region (Table 1).

The average annual seropositivity incidence was highest for HBV (104.6 per 100 000), followed by HCV (78.4 per 100 000), and lowest for HAV (13.6 per 100 000) (Table 2). The eight-year (2000–2007) incidence trends (per 100 000) for HAV, HBV, and HCV seropositivity were studied (Figures 1–3). HAV incidence was almost 7-fold higher in those who were aged <15 years compared to those who were aged ≥15 years (annual average incidence of 27.9 vs. 4.1 per 100 000; $p < 0.001$). HAV incidence was significantly higher in males than females, Saudis than non-Saudis, and in the central and eastern regions than the western region (Table 2). Over these eight years, the incidence of HAV seropositivity decreased by 30% (11.4 per 100 000 in 2000 vs. 8.0 per 100 000 in 2007; Figure 1). When the incidence was stratified by age group, HAV incidence decreased by 42% in those aged <15 years and increased by 61% in those aged ≥15 years. All age groups experienced a markedly increased HAV incidence in 2004 compared to 2003 (outbreak), which was cleared by 2007 in all age groups combined and in those who were <15 years old, but not in those who were aged ≥15 years (Figure 1). HAV incidence followed a seasonal cyclic pattern, with peaks in March and September (Figure 4).

Table 2 Average annual incidence of HAV, HBV, and HCV seropositivity per 100 000 NGHA-served population between 2000 and 2007 by demographic characteristics[a]

	HAV	HBV	HCV
Average annual incidence	13.6	104.6	78.4
Incidence by age group			
<15 years	27.9	5.6	2.8
≥15 years	4.1	169.8	128.2
	$p < 0.001$	$p < 0.001$	$p < 0.001$
Incidence by gender			
Males	14.7	123.0	76.8
Females	12.4	85.5	80.1
	$p = 0.008$	$p < 0.001$	$p = 0.110$
Incidence by nationality			
Saudi	13.7	105.3	76.8
Non-Saudi	7.4	84.0	130.7
	$p = 0.012$	$p = 0.002$	$p < 0.001$
Incidence by NGHA region			
Central	14.2	113.8	99.8
Western	11.4	115.6	59.0
Eastern	15.1	53.8	34.9
	$p = 0.006$	$p < 0.001$	$p < 0.001$

HAV, hepatitis A virus; HBV, hepatitis B virus; HCV, hepatitis C virus; NGHA, National Guard Health Affairs.
[a] Testing differences using the Chi-square test.

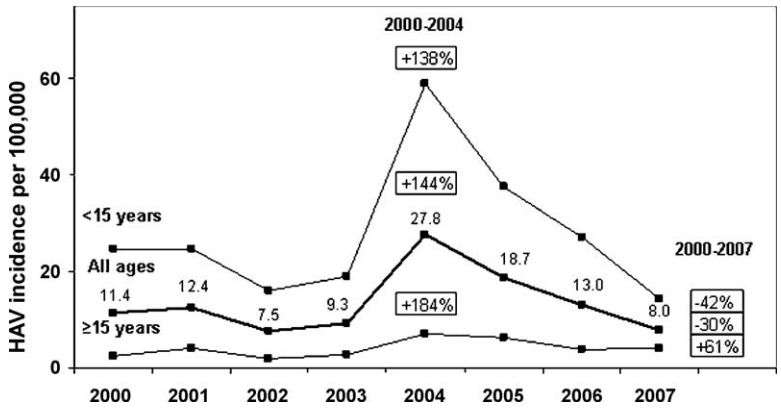

Figure 1 Incidence trends of HAV seropositivity per 100 000 NGHA-served population (by age group) between 2000 and 2007.

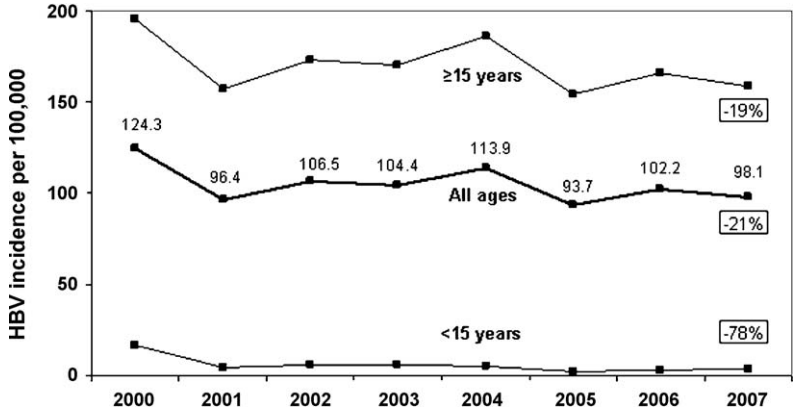

Figure 2 Incidence trends of HBV seropositivity per 100 000 NGHA-served population (by age group) between 2000 and 2007.

The incidence of HBV seropositivity was almost 30-fold higher in those who were aged ≥15 years compared to those who were <15 years (annual average incidence of 169.8 vs. 5.6 per 100 000; $p < 0.001$). HBV incidence was significantly higher in males than females, Saudis than non-Saudis, and in central and western regions than the eastern region (Table 2). Between 2000 and 2007, HBV incidence decreased by 21% for all age groups combined (from 124.3 to 98.1 per 100 000), by 19% for those who were aged ≥15 years (from 195.9 to 158.7 per 100 000), and by 78% for those who were aged <15 years (from 16.7 to 3.6 per 100 000) (Figure 2). There was no clear seasonal variation in HBV incidence (Figure 4).

The incidence of HCV seropositivity was almost 45-fold higher in those who were aged ≥15 years compared to those who were aged <15 years (annual average incidence of 128.2 vs. 2.8 per 100 000; $p < 0.001$). HCV incidence was similar in males and females, but higher in non-Saudis than Saudis and in the central region than in the other regions (Table 2). During the eight-year study period, HCV incidence decreased

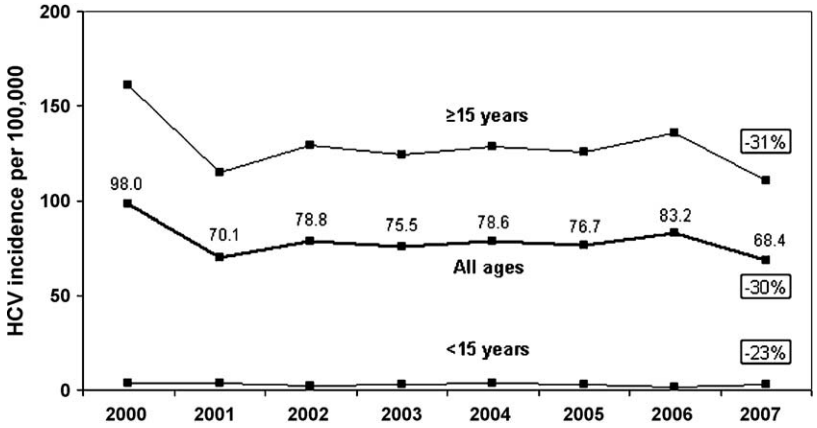

Figure 3 Incidence trends of HCV seropositivity per 100 000 NGHA-served population (by age group) between 2000 and 2007.

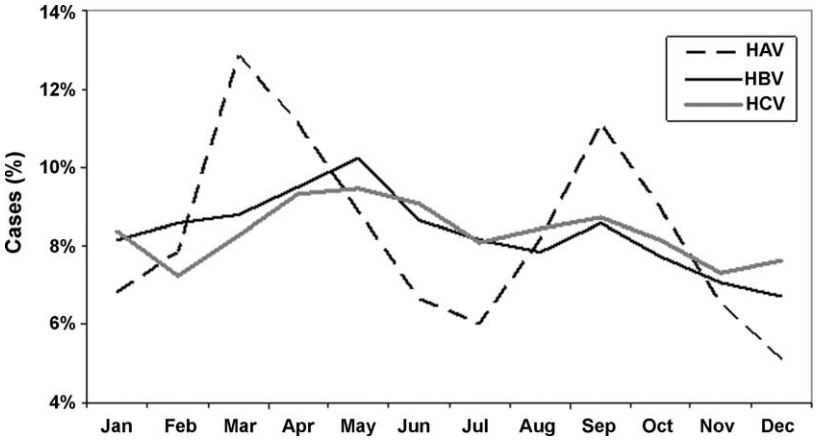

Figure 4 Seasonal variation in the incidence of seropositive cases of HAV, HBV, and HCV reported to the King Abdulaziz Medical City surveillance system between 2000 and 2007.

by 30% (from 98.0% to 68.4% per 100 000). The reduction was generally similar in those who were aged <15 and ≥15 years (23% and 31%, respectively (Figure 3)). There was no clear seasonal variation in HCV incidence (Figure 4).

Discussion

The current study reports for the first time, the eight-year incidence trends of HAV, HBV, and HCV seropositive viral hepatitis in a large population served by the NGHA hospitals in the central, eastern, and western regions of Saudi Arabia. The consistency of the surveillance methodology throughout the study period, including the diagnostic tests used, probably reduces the possibility of biased upward or downward trends. Between 2000 and 2007, the incidence of viral hepatitis seropositivity for all three virus types showed 20—30% declining trends. Similarly, a comprehensive review of prevalence studies of viral hepatitis conducted in Saudi Arabia in the 1980s and 1990s showed a more than 50% decline in all viral hepatitis types.[8] The age group that included children <15 years was that which showed the greatest HBV incidence decline, probably due to the universal infant/child immunization program started in 1990 in Saudi Arabia.[17] The modest HCV incidence reduction, which was similar in those aged <15 and ≥15 years, may be explained by the improved safety of blood products, strict infection control precautions for high risk medical services such as hemodialysis and dental services, enforcing premarital blood screening, and finally increased awareness of dangerous practices such as needle-sharing among drug abusers, cautery, and blood letting. The HAV incidence reduction was driven mainly by the decline in incidence in children aged <15 years who suffered the major part of the disease burden. This reduction may be attributed to the improvements in environmental sanitation that have accompanied major socioeconomic developments in Saudi Arabia over recent decades.[13]

Despite the declines in incidence, the current report confirms that seropositive viral hepatitis, especially that caused by HBV and HCV, remains a major public health problem in Saudi Arabia, and was probably underestimated by the national surveillance system. For example, when comparing the 2007 incidence from this study with the 2007 Saudi MOH data,[1] the incidences of HBV and HCV were 5- to 6-fold higher in our study (98.1 vs. 18.6 per 100 000 for HBV and 68.4 vs. 11.7 per 100 000 for HCV). HAV incidence, on the other hand, was roughly similar (8.0 in our study vs. 5.7 per 100 000), and the 2004 HAV outbreak shown in this report was documented in the Saudi MOH data, at a lower magnitude though.[1] Supporting our observation of national underestimation of HBV and HCV risk in Saudi Arabia, a recent report from the eastern region estimated the average annual incidence as 9.5 for HAV, 46.0 for HBV, and 37.7 for HCV per 100 000 population served by hospitals of the Saudi Aramco Medical Services Organization.[15] Irrespective of the report used, the incidence of seropositive viral hepatitis in Saudi Arabia is remarkably higher than the incidence in the USA,[18] which has one of the world's lowest rates, pointing to the scope of the problem in Saudi Arabia and the need for more comprehensive prevention strategies.

The higher incidence shown in this report may be due to the intensive passive surveillance undertaken in the well-defined NGHA population that occurred in multiple situations, including the recruitment of new military or civilian employees, when medical care for a related condition was sought, during antenatal care (HBV only), in those attending hemodialysis units, in those undergoing organ transplantation or donating blood, or during the conducting of an outbreak investigation (mainly HAV). This exhaustive surveillance may have detected more cases than would be expected from less intensive surveillance, especially as the laboratory-based diagnosis of HBV and HCV used in this and other reports, detects newly developed as well as previously undetected chronic cases. In addition, the incidence of seropositive viral hepatitis could actually be higher in the military population than in the rest of the Saudi population.[19—21]

The current report shows that HBV was the most frequent cause of viral hepatitis seropositivity, followed by HCV, and lastly by HAV. Supporting our findings, prevalence studies on Saudi blood donors over the last decade have shown higher HBV prevalence (1.5—2.6%) compared to HCV prevalence (0.4—1.1%).[11,22,23] However, while the incidence of HAV seropositivity was the lowest among the three studied viral hepatitis types, prevalence studies have consistently shown HAV to be the most prevalent viral hepatitis type. HAV

prevalence was recently estimated to be 29%,[14] which is at least 50% lower than that reported a decade earlier.[13,24] This can be explained by the fact that the surveillance methodology used here and in other surveillance systems, frequently misses many asymptomatic and sporadic cases common in endemic areas. Interestingly, only HAV incidence followed a clear seasonal cyclic pattern, with peaks in March and September. A similar pattern has been described in other countries.[25,26] This may be related to more children being exposed during the mid-year, and summer vacations spent in more endemic areas abroad.

In conclusion, this report describes the incidence trends of seropositive viral hepatitis in a large population from different regions of Saudi Arabia. Over the last eight years, the incidences of all three types of viral hepatitis (caused by HAV, HBV, and HCV) have shown 20—30% declining trends. Nevertheless, the current report confirms that viral hepatitis, especially that caused by HBV and HCV, remains a major public health problem in Saudi Arabia, and has probably been underestimated in previous reports. There is a need for more comprehensive prevention strategies. It is probably going to take two to three decades before viral hepatitis prevalence reflects the full stable effect of any prevention programs. The effectiveness of such prevention programs can best be measured by incidence studies.

Conflict of interest: No conflict of interest to declare.

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